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Relationship of Hemoglobin to Arterial Oxygen Desaturation during Aeromedical Evacuation

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Hypobaric hypoxemia is a well-known risk of aeromedical evacuation (AE). Validating patients as safe to fly includes assessment of oxygenation status as well as oxygen carrying capability (hemoglobin). The incidence and severity of hypoxemia during AE of non-critically injured casualties have not been studied. For this study, subjects deemed safe to fly by the validating flight surgeon were monitored with pulse oximetry from the flight line until arrival at definitive care. All subjects were U.S. military personnel or contractors following traumatic injuries. Non-invasive oxygen saturation (SpO_2), pulse rate, and non-invasive hemoglobin were measured every 5 seconds and recorded to electronic memory. Patient demographics and physiologic data were collected by chart abstraction from Air Force Form 3899, patient movement record. The incidence and duration of hypoxemic events ($SpO_2 < 90\%$) and critical hypoxemic events were determined ($SpO_2 < 85\%$). Sixty-one casualties were evaluated during AE from Bagram Air Base to Landstuhl Regional Medical Center. Mean age was 26.2 ± 6 years, Injury Severity Score was 8 ± 11, and mean SpO_2 prior to AE was 96 ± 2%. The mean transport time was 9.3 ± 1.3 hours. Patients were monitored prior to AE for a brief period, yielding a total recording time of 10.28 hours. The mean hemoglobin at the time of enrollment was 13.2 ± 3.5 g/dL (9.4-18.0g/dL). Hypoxemia ($SpO_2 < 90\%$) was seen in 55/61 (90%) of subjects. The mean duration of $SpO_2 < 90\%$ was 44 minutes. The mean change in SpO_2 from baseline to mean inflight SpO_2 was 4 ± 1.2%. Thirty-four patients (56%) exhibited an $SpO_2 < 85\%$ for 11.7 ± 15 minutes. In conclusion, hypoxemia is a common event during AE of casualties. In patients with infection and concussion or mild traumatic brain injury, this could have long-term consequences.

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TABLE OF CONTENTS

Section **Page**

LIST OF FIGURES

Figure **Page**

LIST OF TABLES

Table **Page**

1.0 SUMMARY

Hypobaric hypoxemia is a well-known risk of aeromedical evacuation (AE). Validating patients as safe to fly includes assessment of oxygenation status as well as oxygen carrying capability (hemoglobin). The incidence and severity of hypoxemia during AE of non-critically injured casualties have not been studied. For this study, subjects deemed safe to fly by the validating flight surgeon were monitored with pulse oximetry from the flight line until arrival at definitive care. All subjects were U.S. military personnel or contractors following traumatic injuries. Non-invasive oxygen saturation (SpO_2), pulse rate, and non-invasive hemoglobin were measured every 5 seconds and recorded to electronic memory. Patient demographics and physiologic data were collected by chart abstraction from Air Force Form 3899, patient movement record. The incidence and duration of hypoxemic events ($SpO_2 < 90\%$) and critical hypoxemic events were determined ($SpO_2 < 85\%$). Sixty-one casualties were evaluated during AE from Bagram Air Base to Landstuhl Regional Medical Center. Mean age was 26.2 ± 6 years, Injury Severity Score was 8 ± 11, and mean SpO_2 prior to AE was 96 ± 2%. The mean transport time was 9.3 ± 1.3 hours. Patients were monitored prior to AE for a brief period, yielding a total recording time of 10.28 hours. The mean hemoglobin at the time of enrollment was 13.2 ± 3.5 g/dL (9.4-18.0g/dL). Hypoxemia ($SpO_2 < 90\%$) was seen in 55/61 (90%) of subjects. The mean duration of $SpO_2 < 90\%$ was 44 minutes. The mean change in SpO_2 from baseline to mean inflight SpO_2 was 4 ± 1.2%. Thirty-four patients (56%) exhibited an $SpO_2 < 85\%$ for 11.7 ± 15 minutes. In conclusion, hypoxemia is a common event during AE of casualties. In patients with infection and concussion or mild traumatic brain injury, this could have long-term consequences.

2.0 INTRODUCTION

The scope and conduct of aeromedical evacuation (AE) dates to, and parallels, the evolution of powered flight. Modern day AE continues to evolve in its doctrine and evidence-based practice. The introduction of the more recent doctrinal term “en route care” (ERC) emphasizes the role of care during medical transport as an opportunity to positively impact and improve the physiology of the combat injured patient during transport [1-3].

In the schema of today’s battlefield, the scope and conduct of AE/ERC begin at the forward area of battle (the site of wounding) to first echelons of care at a battalion aid station or a forward Level II facility such as a forward surgical team or a shock resuscitation team. From this point, the casualty may be moved to an intra-theater Echelon III facility by fixed or rotary wing. In the conflicts of Operation Iraqi Freedom and Operation Enduring Freedom, the theater Level III facility served to render further stabilization care as well as prepare the patient for the strategic evacuation flight to the Level IV facility in Europe [4].

AE policy dictates that a qualified flight surgeon “validate” casualties prior to flight to ensure that the patient is prepared for the rigors of transport. The standards, policies, and processes of the validation are an evolving set of standards established based upon experience, observations and, ideally, evidence-based conclusions. In an ongoing effort to update traditional experiential standards with more objective evidence-based doctrine, the U.S. Air Force School of Aerospace Medicine has continued to fund and encourage research designed to quantify the rigors of the AE process. This study is a result of that process.

One of the major stressors within the AE/ERC continuum is the development and progression of hypoxia and/or inadequate tissue oxygenation (i.e., shock). Hemorrhagic anemia

following wounding may predispose the casualty to the liability of inadequate oxygen delivery. The physiology of inadequate oxygen delivery may be further compromised by the development of hypoxemia as the casualty is transported through a hypobaric environment as cabin altitude ascends during the AE transport process. The normal cabin altitude of strategic AE flights is 8,000 feet above sea level and may affect relative hypoxemia in even normal subjects [5]. The casualty may be more susceptible to hypoxia secondary to atelectasis, hypoventilation (narcotics), altered respiratory mechanics, and/or elevated alveolar/arterial gradient.

Current Air Force AE standards call for correction of anemia in patients with pre-flight hemoglobin of less than 8 g/dL. In addition, AE standards call for the administration of supplemental oxygen and oxygen saturation (SpO_2) monitoring in patients demonstrating pre-flight hypoxemia (defined as $SpO_2 < 92\%$), hypoventilation secondary to narcotic use, or the diagnosis of traumatic brain injury (TBI) [4]. These observations and recommendations are based upon pragmatic experience within the AE community. To our knowledge there has never been a prospective, longitudinal observational study evaluating oxygen saturation during prolonged strategic AE/ERC.

It was our intent to utilize this study to develop objective methodologies to render a more precise and objective understanding of the physiologic stressors that impact upon the AE/ERC casualty during transport. Specifically, we designed a study to continuously monitor SpO_2, pulse rate (PR), and hemoglobin (Hgb) concentrations in a group of wounded personnel who were undergoing strategic AE/ERC from the theater of operations to a Level IV facility in Europe.

3.0 METHODS

The study was approved by the University of Cincinnati Medical Center Institutional Review Board (IRB), the Air Force Research Laboratory IRB, and the in-theater IRB (U.S. Army Medical Research and Materiel Command). Approval for data transfer was also obtained from the Landstuhl Regional Medical Center (LRMC). All U.S. military personnel and civilian contractors requiring AE from Craig Joint Theater Hospital in Bagram, Afghanistan, to LRMC, Germany, who met the inclusion/exclusion criteria, were eligible for enrollment into the study. The study enrolled patients from June 2012 to April 2014. Subject inclusion criteria included the following:

- U.S. military service members and U.S. contractors requiring AE for traumatic injuries received in theater evaluated by the flight surgeon for “fit to fly”
- Age 18-65 years
- Able to provide informed consent
- Ability to have pulse oximetry measured using the second or third digit of either hand
- Heart rate >40 and < 150 bpm
- Systolic blood pressure >90 mmHg

Exclusions for study entry included the following:

- Inability to obtain a reliable pulse oximetry reading due to injuries including burns, amputations, etc.
- Critically ill patients requiring vasopressor support to maintain blood pressure
- Patients requiring mechanical ventilation

- Hypothermia with body temperature < 94°F
- Patients receiving supplemental oxygen prior to transport
- Patients housed in the intensive care unit for severe illness or injury

Patients approved for AE by the validating flight surgeon were screened for enrollment and approached for informed consent. Prior to transport and after informed consent was obtained, a portable pulse oximeter (Rad-57, Masimo Corp., Irvine, CA) was attached to the subject via an adhesive, disposable finger sensor. The oximeter noninvasively measured and recorded arterial SpO_2, PR, Hgb, and pulse index every 2 seconds. The oximeter's screen was covered so as to not alter nurses' normal care of the subjects. Routine spot checks of SpO_2 or continuous SpO_2 monitoring for clinical care were accomplished at the discretion of the AE personnel. Upon arrival to LRMC, the oximeter was removed from the subjects and the data were downloaded to a computer via proprietary software (Trendcom, Masimo Corp., Irvine, CA) and transmitted via secure website to researchers at the University of Cincinnati. Data regarding the subjects' in-flight status and vital signs and care interventions were taken from the Air Force Form 3899, obtained from the Joint Theater Trauma Registry.

Data were cleaned by eliminating data associated with a low pulse index (<1) and missing Hgb or SpO_2 information. All descriptive statistics that were calculated for this study (initial SpO_2, average SpO_2, initial and average Hgb, time monitored) resulted from counts and percentages and the continuous measure of mean. Linear regression analysis was performed to obtain the mean heart rate (HR) for each standard deviation of Hgb concentration. Analysis of variance testing was performed on mean HR in comparison to the previously defined Hgb concentration standard deviation variable. A p-value of <0.001 was obtained for this model.

The statistical software used in the analyses of the study was SAS 9.3 (SAS Institute Inc., Cary, NC).

4.0 RESULTS

In total, 61 casualties were evaluated during AE/ERC transport from Bagram Air Base to LRMC. Table 1 presents basic demographic information characterizing this study group. Average time of monitoring was 617 minutes (10 hours and 17 minutes).

In this study group, 55 of 61 patients (90%) demonstrated at least one episode of hypoxemia as defined by a recorded oxygen saturation of less than 90% (Figure 1). The shortest cumulative time of hypoxemia (saturation < 90%) in any single patient was 4 seconds, while the longest cumulative time of hypoxemia was 233.7 minutes (3.9 hours). The average time with an SpO_2 < 90% for this group of 55 patients was 40 minutes.

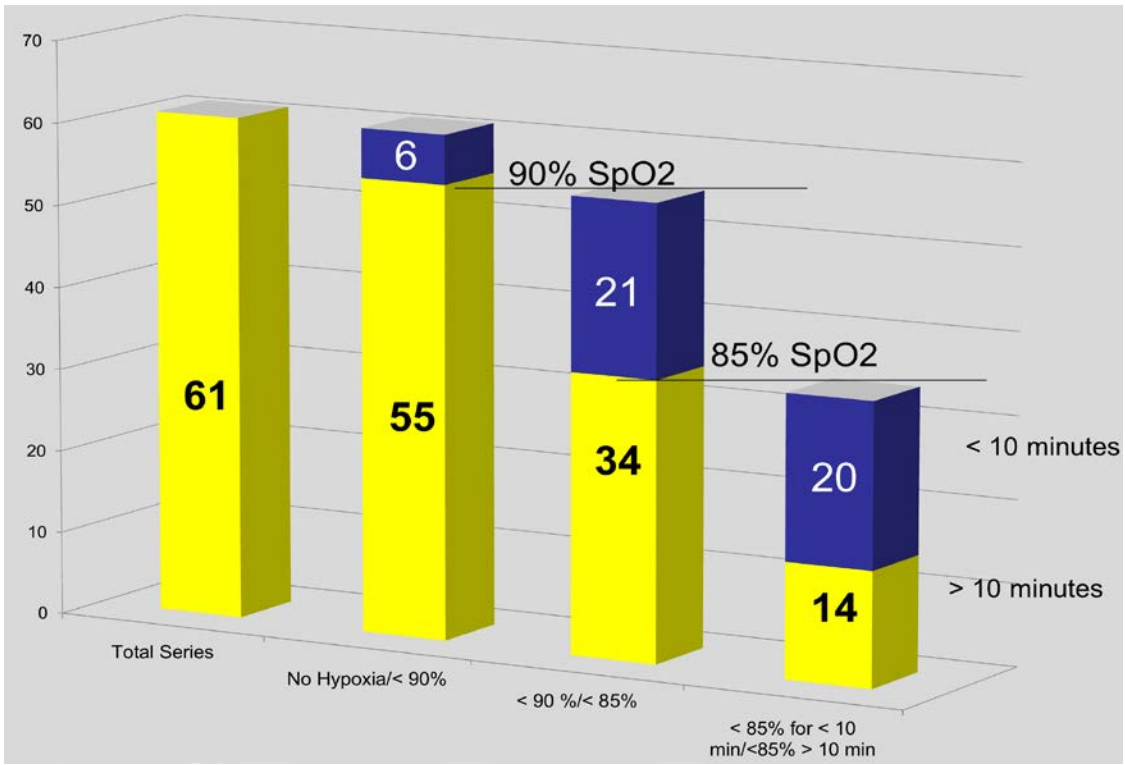
The analysis was repeated for patients with critical hypoxemia. In the study group, 34 of the 61 patients (55%) demonstrated some measurable period of SpO_2 < 85%. The shortest cumulative time of critical hypoxemia was 6 seconds and the longest cumulative time of critical hypoxemia was 42 minutes. The average time with saturation < 85% for this group of 34 patients was 393 seconds (6.5 minutes).

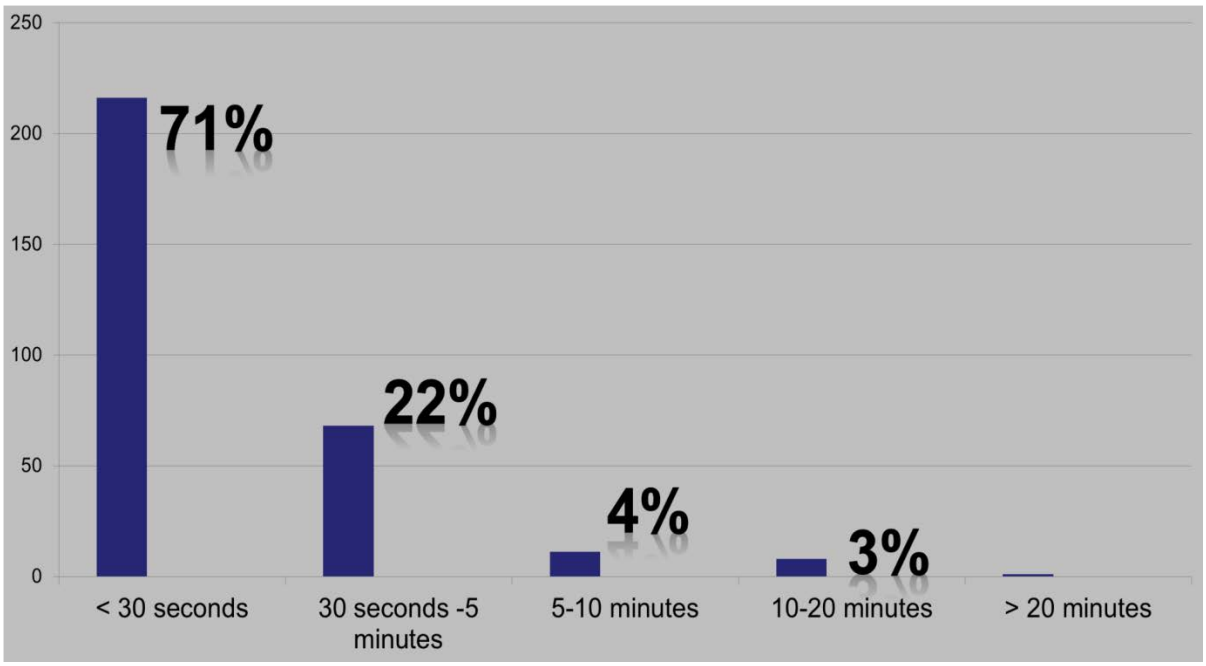
The critical hypoxemia group (n= 34) was divided based upon the average cumulative time of critical hypoxemia extending beyond 10 minutes. Twenty patients demonstrated an average cumulative time of critical hypoxemia less than 10 minutes (2.6 minutes), while 14 patients in this study group (23%) demonstrated an average cumulative period of critical hypoxemia exceeding 10 minutes (24.8 minutes) (Figure 2).

Table 1. Study Participant Demographics

Descriptor	Value
Patients Enrolled	61
Average Age (yr)	26
Service	
Army	44
Marines	11
Air Force	4
Navy	1
Injury Pattern[a]	
IED	27
GSW	14
RPG	4
Grenade	2
Environmental	1

[a]IED = improved explosive device; GSW = gunshot wound; RPG = rocket-propelled grenade.





The study group's initial Hgb was evaluated with respect to HR during the transport period. Initial Hgb prior to transport fell within a narrow range between 10.9 and 15.8 g/dL. HR during transport was analyzed by dividing the group into three categories: Hgb < 12 grams, Hgb 12-15 grams, and Hgb > 15 grams. The results demonstrated a statistically significant increase in HR associated with the lowest Hgb group as compared to the other two groups ($p<0.001$). Patients (n=48) with an Hgb of 12-15 g/dL had a mean PR of 71 bpm, patients with an Hgb < 12 (n=10) had a mean PR of 85 bpm, and patients with an Hgb > 15 g/dL (n=3) had a mean PR of 72 bpm (Figure 3).

Average HRs were compared for patients during periods of hypoxemia (saturation < 90%/mean HR 73) and for periods of severe hypoxemia (saturation < 85%/mean HR 75) as compared to the mean heart rate when patient's saturation were > 90% (mean heart rate 74. There were no statistically significant differences between these groups.

5.0 DISCUSSION

The initial intent of this study included establishing baseline oxygen saturation parameters during AE in a group of U.S. military combat casualties. The results of this trial demonstrate that arterial oxygen desaturation during strategic AE is a more frequent occurrence than originally anticipated. Ninety percent of all patients had at least one event of desaturation below 90%, and 55% of all patients experienced desaturation below 85% during their evacuation. Across a narrow range of Hgb values (10.9-15.8 g/dL), there was no difference in the incidence of hypoxemic events based on absolute Hgb.

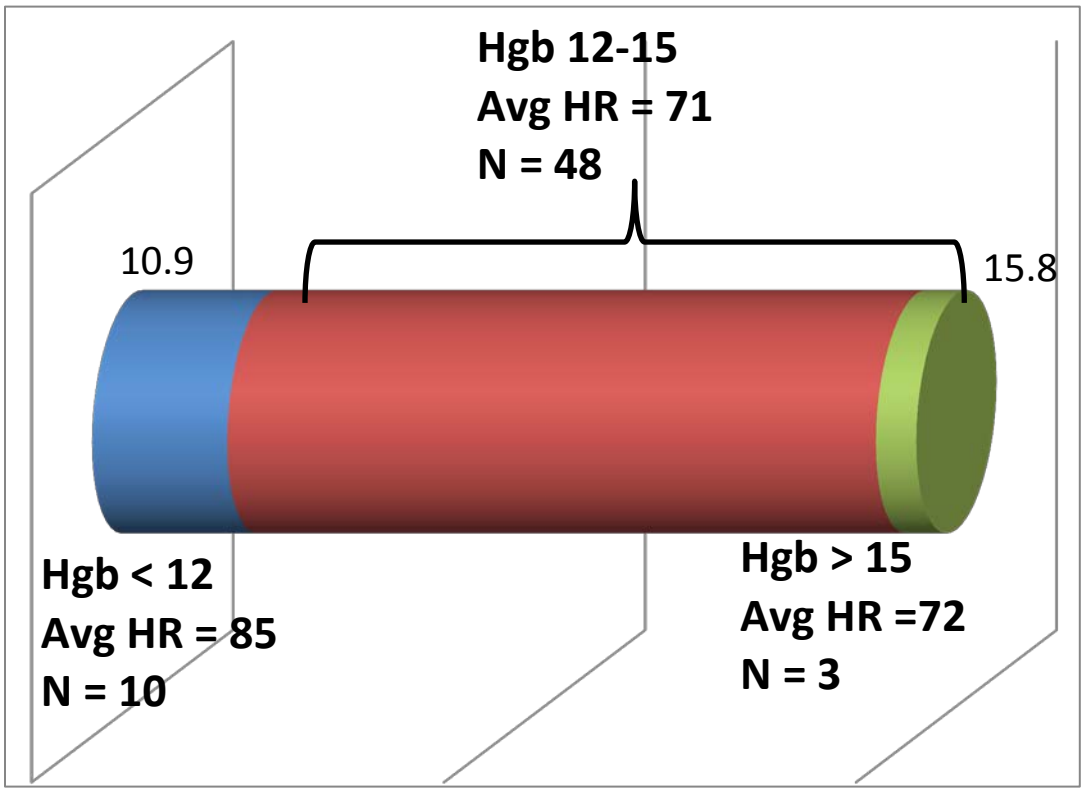


Figure 3. Hemoglobin and heart rate.

In the attempt to ascertain how many of the desaturation episodes were clinically significant, we applied filtering algorithms to the data. Prior to inclusion in the final analysis, the data were examined with respect to the signal integrity from the oximeter. The device utilized in this study (Masimo RAD 57) provides a signal quality parameter (pulse index) for every measurement obtained. The manufacturer suggests that a pulse index of <1 suggests a potentially unreliable receipt of data; therefore, any data point associated with a signal index of <1 was eliminated. We categorized the episodes of desaturation as "hypoxemia" (any SpO_2 < 90%) as well as "critical hypoxemia" (any SpO_2 < 85%). We further characterized the significance of the events by detailing the length of time over which an individual desaturation event transpired. Although a significant number (71%) of the critical hypoxemic events lasted less than 30 seconds, it remains unclear whether even a transient fall to oxygen saturation less than 85% may be injurious to the injured soldier. Of additional concern is the observation that 29% of these episodes lasted longer than 30 seconds, with some documented episodes extending beyond 10 to 20 minutes of critical hypoxemia.

The study was intended to serve as a pilot project to evaluate the physiologic parameters discerned by utilization of a continuous monitoring system as opposed to intermittent and often highly variable documentation by AE crew members. The AE environment is a challenging one and requires the caregiver to maintain situational awareness over a potentially large patient population in the back of an aircraft, which imposes its own set of stressors for maintaining close monitoring of even the most routine patient. This initial study suggests that there is a potentially significant opportunity to improve upon the physiologic monitoring and perhaps the care rendered during AE/ERC.

The observed incidence of hypoxemia is most probably the result of multiple factors interacting during the AE/ERC event. The standard cabin altitude of a strategic AE mission is set at, or about, 8,000 feet. Calculation of the alveolar air equation utilizing a barometric pressure of 564 mmHg yields an alveolar oxygen tension (PaO_2) of 59 mmHg. Even at a normal alveolar to arterial oxygen gradient, PaO_2 would be 55 mmHg. This assumes a partial pressure of carbon dioxide of 40 mmHg and a normal respiratory exchange ratio. Couple this hypobaric hypoxemia with narcotics, sleep, sleep disordered breathing, body position changes, and the residual effects of trauma and surgery, and this observed occurrence of significant hypoxemia is readily explained [5].

The implications of this degree of significant hypoxemia are yet to be fully elucidated. Of obvious concern is the potential impact of this observed level of hypoxemia on patients who have some form of TBI [6-9]. Unfortunately, the study data cannot ascertain the number of patients with a diagnosis of TBI or their long-term outcome. The experience of the authors in the setting of the AE evacuation of this study group would suggest that a portion of this population exposed to a blast mechanism (IED, RPG, and grenade = 32 patients) may have had some element of TBI or post-concussive injury. The other indication for evacuation from theater in patients with battle and blast injuries can be for further neurologic testing at a Level IV facility outside the theater of operations. This is often indicated as the result of failing the cognitive screening process (Military Acute Concussion Evaluation) at the theater hospital and is a reasonably frequent indication for AE movement. There is significant literature available documenting the adverse consequences of even a single event of hypoxemia in the patient with severe TBI. Our group has had a long-standing interest in this topic and recently reviewed the preparation of patients with potential TBI before and during the AE process [9]. Additional investigations will be required to identify specific patients at risk for hypoxemia and TBI during transport. In the interim, it would seem both logical and pragmatic to implement a policy of supplemental oxygen administration as well as oxygen saturation monitoring for any patient who may have had a recent history of TBI and/or concussive injury.

A second group of patients at potential risk for hypoxemic-related complications is those with complex soft tissue wounds. Earnest and colleagues created a caprine model of a contaminated complex musculoskeletal wound based upon initial work of Wenke and others [10-12]. The results of their study demonstrated accelerated bacterial growth when the animals displayed hypoxemia. This bacterial growth was prevented with the application of supplemental oxygen [13]. The potential consequences of this accelerated bacterial growth during hypoxemic conditions are of concern in this patient population since most battle injuries include some form of soft tissue disruption. Further studies will be required to elucidate the potential impact of this relationship.

This study was also intended to evaluate the potential impact of preexisting anemia on patient physiology during AE. The lowest pre-flight Hgb observed in this group was 10.9 g/dL, and the mean initial Hgb for the entire study group was 13.2 g/dL. This range would suggest that an aggressive resuscitation policy is already in place for patients in theater prior to AE transport. This apparent clinical practice standard also limited the ability of this study to evaluate the impact of “conventional anemia” (i.e., Hgb < 7.0 g/dL) since no patients demonstrated this level of anemia. Despite this limitation, the analysis of “relative anemia” demonstrated an association with increasing transport HR as pre-flight Hgb fell. The actual mean HR difference between the low Hgb group and high Hgb group was 13 bpm (71 vs. 84). This difference may be assumed to be of small consequence in this population of otherwise young and previously healthy

battle-injured soldiers. It is important to remember that on occasions the AE and ERC system may be requested to transfer a wide range of critically ill patients who are suffering from non-battle injuries. These patients often include civilians and contractors with issues concerning for myocardial ischemia or myocardial infarction. In this setting it may be important to consider the relative increased HR observed in this study that was associated with relative anemia.

There are a number of limitations to our study. This was a convenience sample of subjects enrolled over an 18-month period. Enrollment was not consecutive, owing to availability of in-theater personnel to consent and apply the device. The retrospective review of the patient movement form (Air Force Form 3899) was complicated by inconsistent documentation and clinical staff charting by exemption. All eligible patients with traumatic injuries were approached for consent, yielding a heterogeneous population. Enrollment was also impacted by changes in the operational environment.

This study demonstrated a much greater occurrence of hypoxemia as well as critical hypoxemia in young, battle-injured soldiers during their AE from a Level III theater hospital to a remote Level IV center. The impact of this hypoxemia remains to be further defined, but may be of particular concern for patients with TBI, concussion, complex soft tissue wounds, and other disease states yet to be defined. The presence of relative anemia prior to AE transport is associated with an increased heart rate during the transport process. In the short term, the occurrence of hypoxemia may be addressed in high-risk patient populations via the provision and administration of supplemental oxygen as well as oxygen saturation monitoring. Further studies remain to be completed to more fully characterize the AE environment and the impact of the AE process on patient physiology.

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LIST OF ABBREVIATIONS AND ACRONYMS

AE	aeromedical evacuation
ERC	en route care
Hgb	hemoglobin
HR	heart rate
IED	improvised explosive device
IRB	Institutional Review Board
LRMC	Landstuhl Regional Medical Center
PaO_2	aveolar oxygen tension
PR	pulse rate
RPG	rocket-propelled grenade
SpO_2	oxygen saturation
TBI	traumatic brain injury